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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,453	01/03/2006	Eugene Tedeschi	PA1751	8045

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MEDTRONIC VASCULAR, INC.
IP LEGAL DEPARTMENT
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EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
09/11/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

rs.vasciplegal@medtronic.com

Office Action Summary	Application No.	Applicant(s)	
	10/563,453	TEDESCHI, EUGENE	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *9,10,15-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11-14,17-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restriction filed on July 27, 2007 is acknowledged. Claims 1-25 are pending in this application.

Restriction

1. Applicant's election without traverse of proteasome inhibitor species bortezomib and the polymer species acrylic polymers and copolymers in the reply filed on July 27, 2007 is acknowledged. A search was conducted on elected species of a medical device comprising a stent delivering bortezomib, and a prior art was found. A search was conducted on elected species of acrylic polymer as the polymer coating the surface of the stent, and this appears to be free of prior art. A search was extended to the other polymer species, and prior art was found. Claims 9-10 and 15-16 are withdrawn from further consideration, as being drawn to nonelected species. Claims 1-8, 11-14 and 17-25 are examined on the merits in this office action.

Objection-Minor Informalities

2. The title is objected to because the title is too long. The title is limited to 2-7 words maximum. A new title is required that is clearly indicative of the invention to which the claims are directed.

3. The specification is objected to because of a spelling error. At paragraph [0012] line 3, "bortezomib" is misspelled as "bortezomdib". This error should be corrected. Please correct all possible spelling errors that may be in the specification.

Rejection-35 U.S.C. 112, 2nd

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 6 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 6 recites the limitation "the normal" in the last line of the claim. There is insufficient antecedent basis for this limitation in the claim.

Rejection-35 U.S.C. 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1, 4, 6-8, 12, 20-21 and 23-25 are rejected under 35 U.S.C. 102(e) as being anticipated by Epstein SE (PG Pub 2004/0116329) as evidenced by Adams J (Expert Opinion Ther. Patents, 2003, 13(1): 45-57).

9. The instant claims are drawn to a medical device for delivering an anti-restenotic composition comprising: a stent having a generally cylindrical shape comprising an outer surface, an inner surface, a first open end, a second open end and wherein at least one of said inner or said outer surfaces are adapted to deliver an anti-restenotic

effective amount of at least one proteasome inhibitor to a tissue within a mammal, and the proteasome inhibitor is bortezomib. The claims are further drawn to a method for inhibiting restenosis in a mammal comprising the site specific delivery of at least one proteasome inhibitor, wherein said proteasome inhibitor is delivered to a site at risk for restenosis using a vascular stent, and the proteasome inhibitor is bortezomib.

10. Epstein SE teaches inhibition of restenosis of blood vessels by administering to the cells in the blood vessel walls a compound, e.g., a protein or small molecule, capable of inhibiting the ubiquity-proteasome protein degradation pathway. The inhibiting compound is preferably administered by coating the compound on a stent and implanting the stent in the blood vessel after angioplasty (see abstract). The reference further teaches the inhibition of restenosis by inhibiting a new target within the cells responsible for the stenotic proliferation of tissue in order to prevent the multiple processes involved in restenosis (see paragraph [0027]). Furthermore, the reference teaches inhibition of cell proliferation, particularly of smooth muscle cells in arterial walls is achieved by inhibiting the ubiquitin-proteasome protein degradation pathway, thereby interfering with proliferation of cells that could contribute to restenosis (see paragraph [0028]). The reference teaches that LDP-341 is described as a proteasome inhibitor (see paragraph [0037]). As evidenced by Adams J, the proteasome inhibitor bortezomib (Velcade) is also known as PS-341, MLN-341 and LDP-341 (see p. 45, 2nd paragraph). The reference claims an intravascular stent coated with a compound capable of inhibiting the ubiquitin-proteasome protein degradation pathway in a cell (claim 5) and the stent of claim 5 wherein said compound is LDP-341 (claim 6). This reads on claims

1, 4, 6-8 and 12. Furthermore, the reference claims a method of preventing cell proliferation in blood vessel walls after angioplasty comprising administering to at least one cell in a blood vessel wall after an angioplastic procedure an amount of a compound capable of inhibiting the ubiquitin-proteasome protein degradation pathway in the cell effective to prevent proliferation of the cell, wherein the compound is LDP-341, and the compound is administered by coating the compound (LDP-341) on a stent and implanting the stent within the blood vessel (see claims 1-4). This reads on claims 20-21 and 23-25. The specification of instant application discloses that the effective amounts of proteasome inhibitors can be determined by a titration process. Generally, and not intended as a limitation, an anti-restenotic effective amount of the proteasome inhibitors will range between about 0.5 ng to 1.0 mg depending on the particular proteasome inhibitor used and the delivery platform selected (see paragraph [0052]). Thus, "an effective amount" has been treated as test-by-test case, and the prior art teaches that compound administered via a stent-based platform, by achieving high local concentrations at the vessel wall and low systemic concentrations, will be effective with minimal systemic side effects (see paragraph [0039]). Furthermore, the reference teaches that any stent coating that has the proper release kinetics for the proteasome inhibiting protein, small molecule, or gene encoding such a product, and that allows for viable incorporation of such a molecule, and that allows for such product to reside in the coating for days or weeks, will be appropriate (see paragraph [0044]). Although the reference is silent as to the shape of the stent, the reference discloses that the stent is implanted into the blood vessel, and therefore is tubular, and because it is tubular, it

would have a cylindrical shape having an outer and an inner surface. Therefore, the prior art meets the limitations of claims 1, 4, 6-8, 12, 20-21 and 23-25.

Rejection-35 U.S.C. 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. Claims 2-3, 5, 11, 13, 14, 17-19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Epstein SE (PG Pub 2004/0116329) as evidenced by Adams J (Expert Opinion Ther. Patents, 2003, 13(1): 45-57) as applied to claims 1, 4, 6-8, 12, 20-21 and 23-25 above, and further in view of Palasis et al (PG Pub 2004/0106987).

14. The instant claims are drawn to a medical device for delivering an anti-restenotic composition comprising a stent, wherein the stent is mechanically and self expandable and delivered to anatomical lumen using a balloon catheter, and the surface of the stent

is coated with a polymer wherein the polymer has at least one proteasome inhibitor incorporated therein.

15. As described supra, Epstein SE teaches inhibition of restenosis of blood vessels by administering LDP-341 on a stent and implanting the stent within the blood vessel. The difference between the reference and the instant claims are that the reference does not teach expandable stent, polymer coating wherein the proteasome inhibitor is in a concentration of between 0.1% to 99% by weight of proteasome inhibitor-to polymer, balloon catheter, delivery of proteasome inhibitor to a site at risk using injection catheter.

16. However, Palasis et al teach a medical devices for delivery of therapeutic agents and at least one polymeric layer, which typically acts to control the release of the therapeutic agent from the medical device (see abstract). Furthermore, the reference teaches that biostable polymeric covering layers include those that comprise one or more of the following: polyolefin polymers and copolymers, ethylenic copolymers, polyurethane polymers and copolymers...(see paragraph [0016]). The reference further teaches that the polymer coated endovascular stent having a conventional frame, such as tubular shape, and permits the stent to self-expand or to expand to the desired shape after an expansive force is applied, for example, by the expansion of a balloon within the stent (see paragraph [0061]). The reference teaches that a coating is applied on the surface of each stent, and the coating can include either a biostable or biodisintegrable polymer which contains or is provided as a coating over a therapeutic agent (see paragraph [0062]). Furthermore, the reference teaches that numerous

therapeutic agents that have been identified as candidates for vascular treatment regimens, such as agents targeting restenosis can be used on the medical device, including proteasome inhibitor (see paragraph [0072]).

17. Therefore, it would have been obvious to one of ordinary skilled in the art to combine the teachings of Palasis et al and Epstein SE, since they both teach a medical device, stent (with a coating that has the proper release kinetics), delivering a therapeutic agent (especially to inhibit restenosis) to the treatment site. There is a reasonable expectation of success since devices as stents have limited surface areas (see Palasis paragraph [0007]), and thus polymer coating containing a therapeutic agents will provide adequate control of the release of that therapeutic agent (see paragraph Palasis [0010]). Additionally, polymer coated medical devices such as stents, containing therapeutic agents can be provided in which the rate of release of the therapeutic agents is adequately regulated so as to provide a therapeutically effective amount of such agent over a desired period of time (see paragraph [0032]); can be provided in which the polymer resists cracking upon expansion of the medical device (see Palasis paragraph [0033]); can be provided wherein the structural integrity of the therapeutic agent is not substantially disrupted during medical device manufacturing (see Palasis paragraph [0034]); and can be provided in which the uptake of the therapeutic agent by the targeted tissue is enhanced (see Palasis paragraph [0035]).

18. Furthermore, It has been held that under KSR that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in KSR, When there is motivation "to solve a problem and there are a finite number of identified, predictable

solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727,_,82 USPQ2d 1385, 1397 (2007).

19. The "problem" facing those in the art was alleviating restenosis after surgical intervention by means of balloon angioplasty or bypass grafting, and there were a limited number of methodologies available to do so, for example a catheter delivery systems and coated stents to deliver proteins or small molecules (coating impregnate with therapeutic agents). The skilled artisan would have had reason to try these methodologies with the reasonable expectation that at least one would be successful. In this case, because the LDP-341 is a proteasome inhibitor, and coating the stent with polymer can provide therapeutically effective amount over a desired period of time, and both were useful for inhibiting restenosis. Thus, inhibiting restenosis using bortezomib (proteasome inhibitor) coated within a polymer in a concentration of between 0.1% to 99% by weight on a stent is a "the product not of innovation but of ordinary skill and common sense," leading to the conclusion that invention is not patentable as it would have been obvious.

Conclusion

20. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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9/4/07
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